• Summary

Gene expression and its control are central to the understanding of all complex biological processes. Over the past several decades, the control of gene expression at the transcriptional level has received much attention, and its essential principles are now well established. More recently, there has been a rapidly growing interest in understanding the control of both normal and disease-associated gene expression at the posttranscriptional level. Such control is diverse and complex, involving the steps of transcription elongation and termination, nuclear pre-mRNA processing, the export of nuclear mRNA to the cytoplasm, the initiation and elongation of cytoplasmic mRNA translation, cytoplasmic mRNA decay, as well as the RNA structures and the diffusible RNA and protein factors that regulate these events.

Several new and very important principles are now emerging from this rich body of work, all of which apply to prokaryotic and eukaryotic organisms. RNA structure is believed to influence nearly every step of posttranscriptional gene expression. New data bearing on higher order RNA structures, atypical nucleotide interactions, and the kinetics and pathways of RNA structure formation are now emerging. The rapidly evolving concepts of RNA structure and function reflect the speed with which advancements are being made and are predictive of future abilities to understand and manipulate RNA structures in order to understand and manipulate gene expression.

In addition to the principles of RNA structure are the emerging principles of RNA-protein interactions, which appear to differ substantially from the well-defined DNA-protein interactions that promote and control gene transcription. While primary sequences in RNA may be important, in many cases the specificity of RNA-protein interactions rests largely on conserved structural features of the RNA rather than on the RNA sequence per se. A better understanding of RNA-protein interactions most likely will depend upon a better understanding of the details of RNA structure formation and stability, and vice versa.

The in vitro design and selection of an RNA binding or enzymatic activity from a randomized library of RNA sequences is also an upcoming area of research. The selectability of RNAs as epitopes that are immunologically cross-reactive to specific peptides has broad implications to drug design in the treatment of cancer, AIDS, autoimmunity and heritable disease.

The goal of this international meeting is to bring together a broad range of geneticists, molecular biologists, chemists, biochemists, and evolutionary biologists working on the posttranscriptional control of gene expression as well as the selection of RNA binding or enzymatic activities. Formal research presentations will be combined with less formal roundtable discussions in order to promote the free exchange of research information and the critical discussion of ideas and controversies in the rapidly developing fields of RNA structure and function.

- **Statement of Need**

The meeting will focus on the diverse reactions that comprise the posttranscriptional steps of gene expression. It will also address the potential applications of RNA to drug design in treating disease and in understanding the evolution of life as we know it. Inherent to all presentations will be the aim to understand more completely the relationship between RNA structure and RNA function. The research challenges that lie ahead include identifying the cis-acting structures and trans-acting factors that mediate posttranscriptional control. RNA, in contrast to DNA, plays multi-faceted roles in the cell. RNA can serve as a substrate for RNA processing, contain sequences necessary for transport across the nuclear envelope, encode protein, and contain determinants of half-life. RNA can also constitute autocatalytic sequences, termed ribozymes. Furthermore, certain small nuclear RNAs can function in complexes with proteins to remove introns from pre-mRNA or trim the 3' end of pre-tRNA. The active roles of RNA as substrates as well as cis- and trans-acting effectors of posttranscriptional processes probably reflect a past primordial world in which RNA was the progenitor of both DNA and protein.

To our knowledge, this meeting is distinct from all meetings that have been held within at least the past two years or that are planned for the future because this meeting will bring together scientists who study the diverse yet fundamentally-related steps of posttranscriptional control, beginning with transcription termination and ending with protein synthesis and mRNA decay. This meeting will begin to address the temporal and physical coordination of the individual steps within the cell. This meeting will also have a session on the combinational selection of RNA binding or enzymatic activities and the evolution of RNA function. For the first time, cellular, molecular, structural and evolutionary biologists who are interested in RNA structure and function will be able to convene and achieve an appreciation of the biology of RNA from a breadth of perspectives.

This will be a well-attended and important conference that will provide an opportunity for investigators from all over the world to assemble and discuss the most recent advances in understanding posttranscriptional processes. Many of the people who will attend this meeting might normally spend their limited travel funds to attend a meeting that focuses on one or a few of the posttranscriptional processes that define their research. It is our goal to bring these people together in order to share experimental findings and common problems. Considering our current list of participants, most of whom are established investigators, we now aim to solicit the participation of young lab heads and post-doctorals. The travel and living expenses of these individuals will be given priority for CTR funding. The expenses of all others will be considered secondarily on the basis of financial need. Currently, women comprise 12% of the program. This percentage will be increased by inviting more women at both the junior and senior levels.

- **Topics and Chairpersons of the Conference**

Topic	Chairperson
Transcription termination/antitermination, including the role of antisense RNA	Terry Platt
RNA splicing, RNA ribozymes in splicing and other reactions	Christine Guthrie
Translational fidelity and ribosome frame-shifting	Mike Tuite
The control of mRNA translation	Debbie Steege
mRNA stability in general and as a consequence of mRNA translation	Lynne Maquat
The structure and function of ribonucleoproteins, including ribosomes	Harry Noller
RNA structural analyses including structure formation and stability	Ignacios Tinoco
The in vitro selection of an RNA structure or function	Larry Gold

- **Recent Meetings on the Same Subject**

To our knowledge, this meeting will be unique relative to past or planned meetings in the sense that it will consider the full range of posttranscriptional processes. These processes will be examined individually as well as with respect to how they are choreographed temporally and physically in the cell to comprise a single pathway. The roles of RNA structure and trans-acting factors in the component reactions will also be considered as will the chemistry of the reactions.

Examples of meetings that have or will overlap with this meeting include the following:

Title	Place and Date
Cytoplasmic Aspects of the Post-Transcriptional Regulation of Gene Expression	La Londe-les-Maures, France, March 28-April 2, 1993
RNA Processing, Cold Spring Harbor Labs	Cold Spring Harbor, New York, May 19-23, 1993
RNA 3' End Formation	Oxford, UK, September 15-19, 1993
International Symposium on RNA Processing and Nucleo-Cytoplasmic Transport	Marburg, FRG, October 12-14, 1993
RNA Processing, Cold Spring Harbor Labs	Madison, WI, May 24-29, 1994

- **Members of Organizing Committees**

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- **Proposed Participants, Location, Probable Dates, Method of Invitation**

Proposed list of Speakers	Commitment*
<u>Antisense RNA/(Anti)termination</u> (3)	
T. Platt (USA)	+++
R. Simons (USA)	+++
G. Wagner (Sweden)	+
<u>RNA splicing/ribozymes</u> (2)	
N. Pace (USA)	+++
C. Guthrie (USA)	+++
<u>Translational fidelity and frameshifting</u> (4)	
M. Tuite (UK)	+++
A. J. Kingsman (UK)	+++
S. Pedersen (Denmark)	+
H. Engelberg-Kulka (Israel)	+++
<u>Translation and Translational control/ regulation</u> (27)	
J. E. G. McCarthy (FRG)	+++
T. F. Donahue (USA)	+++
A. E. Dahlberg (USA)	+++
J. van Duin (Holland)	+++
T. D. Fox (USA)	+++
M. Dreyfus (France)	+++
A. Hinnebusch (USA)	+++
C. Gualerzi (Italy)	+
M. Kozak (USA)	+++
J. Hershey (USA)	+++
A. Oppenheim (Israel)	+++
M. B. Mathews (USA)	+++
G. Thireos (Greece)	+++
N. Sonenberg (Canada)	+++
A. Böck (FRG)	+++
H. Trachsel (Switzerland)	+
R. Klausner (USA)	+++
Y. Nakamura (Japan)	++
B. Ehresmann (France)	++
R. Jackson (UK)	+++
P. Sarnow (USA)	+++
M. Wickens (USA)	+
D. Draper (USA)	+++
C. Proud (UK)	+++
D. Steege (USA)	+++

I. Boni (Russia)	++
P. Walter (USA)	+++

mRNA stability (13)

J. G. Belasco (USA)	+++
C. F. Higgins (UK)	+++
S. N. Cohen (USA)	+++
A. von Gabain (Sweden)	++
A. Jacobson (USA)	+++
M. Grunberg-Manago (France)	+++
A. Sachs (USA)	+++
R. Parker (USA)	+++
S. Peltz (USA)	+++
D. W. Cleveland (USA)	+++
F. Lacroute (France)	+
J. Ross (USA)	+++
G. Brewer (USA)	+++
L. E. Maquat (USA)	+++

RNA structural analysis/ribosomes (3)

I. Tinoco (USA)	+++
R. Brimacombe (FRG)	+++
H. Noller (USA)	+++

In vitro selection of RNA (5)

L. Gold (USA)	+++
G. Joyce (USA)	+++
O. Uhlenbeck (USA)	+
J. Keene (USA)	+++
J. Szostak (USA)	+++

*Commitment for each speaker indicated as follows:
+++ definitive
++ tentative
+ awaiting reply

Location

The Hyatt, Aruba, The Dutch Antilles. Aside from being an attractive and centrally located place to draw high quality scientists, this resort was chosen because it will be very conducive to interactions between scientists. All participants will reside and take meals together. The resort is sufficiently isolated from attractions other than those of nature so that participants will be inclined to interact outside of the formal sessions. All facilities are accessible to any disabled participant.

Dates

April 28 - May 3rd, 1994 (the beginning of off-season, when rates are reduced).

Method of Invitation

The individuals listed above have already been contacted by letter and phone. We believe that our ability to develop such a list of outstanding scientists is the result of (1) the novel breadth of the RNA processes to be discussed, (2) the format of formal talks that are no less than 20 minutes plus supplemental informal roundtable discussions, and (3) the appealing location and time of the meeting. Additional speakers and participants will be selected from individuals who respond to advertisements of the meeting. Advertisements will be placed in journals including Science and Nature. We aim to recruit young lab heads and post-doctorals through advertising. These individuals plus the junior faculty members who are already invited will be given priority for CTR funding on the basis of need. Two of the six organizers and three of the eight chairpeople are women, and 7 of the current 57 participants are women. We aim to increase the number of women participants so that ratio of women to men participants reflects the ratio of women to men scientists. This will be done for speakers, young lab heads and post-doctorals.

• Budget

		Proposed subsidies to individuals (No. x Average amount)	Overall Estimated Costs	Support Requested from the CTR
(1)	Transportation expenses invited speakers			
	- from USA/Canada	35 x $500	17,500	
	- from Europe/Scandinavia/ Japan/Israel	21 x $750	15,750	
	Other participants (ave) -	8 x $600	4,800	1,800[1]
		(No. x average amount)		
(2)	Per diem living expenses (5 days/nights @ $158/double room each night and $60/meals each day) -	80 x $695	55,600	2,085[1]
(3)	Rentals (conference rooms, equipment)		500	
(4)	Clerical and technical assistance (projectionist, meetings secretary)		500	
(5)	Organizational expenses			
	- advertisements		1,000	
	- mail, telephone, fax		500	
		Estimated total cost	$96,150	$3,885

[1]for 3 participants

- **Support Currently Available or to be Requested**

Available

The NATO International Scientific Exchange Programmes has committed $17,800 to this meeting.

Requested

In addition to The Council for Tobacco Research, funds will be solicited from the NSF, the NIH and the business sector of the scientific community. Lists of companies that have provided financial support for other scientific meetings have been obtained from colleagues. A letter has been drafted that explains the needs and goals of our meeting. The letter has been mailed together with the list of current participants and a sample fax form on which the company can readily check the option to contribute and provide the name of a fiscal administrator for future contact.

All participants who are established investigators and who are able to provide all or a percentage of their meeting expenses will be asked to do so.

- **Organization of Meeting, Dissemination of Results, Contributions of Results**

The meeting will be organized into morning and evening sessions of either talks or roundtable discussions. The talks will be 20 minutes and will be followed by a 5-10 minute question-and-answer period. Each talk will fall under one of the topics listed on page 3 of this application. The roundtable discussions will be broader in perspective and will aim to address new and emerging themes of the meeting as well as experimental and conceptual difficulties that are in need of resolution. Like the sessions, they will be chaired by one individual. Approximately four individuals will be designated participants, yet the floor will be open to any member of the meeting.

In order to maximize dissemination of the results of the meeting, only one member from each laboratory will be accepted into attendance. Furthermore, participants will derive from at least 15 countries, the number of countries represented by current participants. Scientists at all levels of career development will be invited, including post-doctorals, junior faculty and established investigators. Additionally, the organizers anticipate publishing a review of the meeting in a widely-read journal. Published material will acknowledge support provided by The Council for Tobacco Research.